UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/716,531	09/19/96	MAHE Y	016800-111

18M1/0915

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ART UNIT	PAPER NUMBER
1806	6

DATE MAILED: 09/15/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

☆U.S.GOVERNMENT PRINTING OFFICE 1995-319-826

Office Action Summary	Application No. 08/716,531	Applicant(s) Mahe et al
	Examiner Sheela J. Huff	Group Art Unit 1806

☒ Responsive to communication(s) filed on *Jul 10, 1997*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11 and 16-19* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11 and 16-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. The amendment filed on 7/10/97 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

   Claims 12-15 have been cancelled.

   Claims 16-19 have been added.

   Claims 1-11 and 16-19 are pending.

2. The rejection under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendments.

3. The objection to the specification and claim 4 is withdrawn in view of applicant's amendment.

Response to Arguments

Claim Rejections - 35 USC § 112

4. Claims 1-11 and 16-19 remain/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of tripeptides K(D)PV, does not reasonably provide enablement for peptides that "contain" said tripeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons for this

rejection are of record in paper no. 4, mailed 4/21/97. It is noted that both "contain" and "comprise" are known to be language and equivalent terminology.

Applicant argues that undue experimentation would not be required to determine which of the peptides "comprising" the tripeptide would be effective as an anti-inflammatory. If the peptide were limited to having the anti-inflammatory function, then applicant's arguments would be persuasive. However, such a limitation is not in the claimed. As stated in paper no. 4, a functional limitation in the body of the claim would help overcome this rejection.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ferreira et al US 5389615 or Oluyomi et al Eur. J. Pharm. vol. 258 p. 131 (1994). The reasons for this rejection are of record in paper no. 4, mailed 4/21/97.

Applicant argues that each of the primary references is directed to the treatment of pain and that pain cannot be equated to inflammation. The Examiner disagrees. With respect to Ferreira, applicant argues that pain can be caused by a number of causes other than inflammation, such as trauma, burns etc. It is well known that one of the characteristic pathologies of inflammation is pain (see Stedmans' Medical Dictionary 24th edition p. 707-708 (1989)). In cases such as trauma and burns, inflammation is generally also involved. Furthermore, in col. 1, lines 10-30, the reference discloses that IL-1β is involved in a number of inflammatory diseases and that a number of peptides have been discovered that antagonize such activities (the discovered peptides are analgesics). The reference goes on to state that lys-D-pro-val antagonizes hyperangelsia (col. 4, line 29) (ie that the peptide is an analgesic). It is also noted that the reference compares the analgesic activity of the tripeptide to the analgesic activity of indomethacin. As disclosed in Merck, 11th edition p. 4869-4879 (1989), indomethacin is a known anti-inflammatory agent. Thus, the reference and the state of the art equate pain and inflammation.

With respect to Oluyomi et al, applicant argues that the reference teaches anti-nociceptive activity and that this is not inflammation. The reference compares the activity of indomethacin to the tripeptide and as states above indomethacin is a known anti-inflammatory agent. Furthermore, the reference states that the peptide analogs containing the dipeptide lys-pro "constitute a novel approach to the control of pain,

particularly **inflammatory** pain" (emphasis added, p. 131, second column, first full paragraph). The reference also states that the peptide inhibit the release of prostaglandin and other inflammatory substances (p. 136, first column, lines 5-9 from the bottom). Additionally, on page 137, first column, lines 8-11, the reference states "this confirms the peripheral anti-inflammatory activity of this peptide" (this peptide refers to lys-D-pro-val-NH2). Thus, contrary to applicant's response, the reference is dealing with the treatment of inflammation.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 4, 7-10 and 18 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferreira et al US 5389615 as applied to claims 1-3 above. The reasons for this rejection are of record in paper no. 4, mailed 4/21/97.

Applicant again argues that pain is not inflammation. Applicant is directed to the above responses. Additionally applicant argues that hyperalgesia is not inflammation but sensitivity to pain. As stated above, the reference is treating inflammation.

10. Claims 5-6 and 19 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferreira et al US 5389615 as applied to claims 1-3 above further in view of Lipton US 5157023 and Oluyomi et al Eur. J. Pharm.. vol. 258

p. 131 (1994). The reasons for this rejection are of record in paper no. 4, mailed 4/21/97.

Applicant argues that pain is not inflammation and that Lipton does not cure this deficiency. Applicant's arguments have been addressed above. Since there are no deficiencies in the primary reference with respect to pain/inflammation, there are no deficiencies to cure.

11. Claims 1-11 and 16-19 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferreira et al US 5389615 in view of Nordlund et al US 4874744, Lipton US 5157023 and Remington's Pharmaceutical Sciences, 16th Ed. (1980), CH 87 and 92 and Oluyomi et al Eur. J. Pharm.. vol. 258 p. 131 (1994). The reasons for this rejection are of record in paper no. 4, mailed 4/21/97.

Applicant argues that inflammation may result in pain and that inflammatory responses do not always elicit pain. This is merely a statement and there is no evidence of record to substantiate this. In view of the Examiner's rebuttal (see above), the Examiner disagrees.

Applicant argues that Nordlund et al, Lipton, and/or Remington's fail to teach the treatment of inflammation. As discussed above, the primary reference does and the

secondary references were cited to show that topical formulations and protecting groups are known in the art.

12. Claims 1-3, 5-11 and 16-19 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Oluyomi et al Eur. J. Pharm.. vol. 258 p. 131 (1994) in view of Nordlund et al US 4874744, Lipton US 5157023 and Remington's Pharmaceutical Sciences, 16th Ed. (1980), CH 87 and 92. The reasons for this rejection are of record in paper no. 4, mailed 4/21/97.

Applicant's arguments have been addressed above.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

~~13.~~ Claims 5-6 and 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claim 5, line 4, the terminology "end-terminal" is vague and indefinite. Does applicant mean --N-terminal--?

b. Claims 16-19 should refer to the independent claim in a definite manner. For example, in claim 16, line 1 "A" should be --The--.

Conclusion

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Applicant is directed to the claims of Ferreira et al US 5580855.

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is (703) 305-7866. The examiner can normally be reached on Monday-Thursday from 6:30am to 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703)308-2731. The FAX phone number for this Group is (703)308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**lila.feisee@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. **PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122.** This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Sheela J. Huff
September 11, 1997

Sheela J. Huff
Patent Examiner
Group 1800